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ORIGINAL ARTICLE

Protective potential of *Tetrapleura tetraptera* against trona (*kaun*) -induced hepatic injury in rat models

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Abstract

The antioxidant protective effect of the fruits and peels of *Tetrapleura tetraptera* were investigated in trona (*kaun*)-induced oxidative injuries in male albino rats. The peels and fruits of *T. tetraptera* were air-dried and extracted with ethanol. The concentrated extracts were subjected to FTIR spectroscopy analysis to identify their chemical functional groups. Five groups of six rats each were pretreated with trona (500 mg/kg bw) for 7 days, while a sixth group was administered water only which served as normal control. Four of the pretreated groups were subjected to posttreatment with *T. tetraptera* extracts, while the fifth served as negative control. At the end of the experiment, their hepatic, kidney, and intestinal tissues were assessed for catalase activity and malondialdehyde (MDA) level. Aspartate transaminase (AST) and alanine transaminase (ALT) levels were analyzed in blood serum. While histopathology was carried out on hepatic tissues. FTIR spectroscopy of the extracts revealed amines, alcohols, carboxylic acids, esters, ethers, aromatics, alkanes, aldehydes, ketones, phenols, and amides as the functional groups. Ingestion of trona caused significant ($p < 0.05$) increase in all studied biological parameters in all tissues. These were significantly ($p < 0.05$) reversed to near normal after treatment with both extracts. Histopathology revealed reduction in trona-induced lesions and alterations in hepatic tissue after treatment with the extracts. These results indicate the antioxidant protective effect of *T. tetraptera* against trona-induced oxidative injury, which can be attributed to the identified functional groups.

Keywords Antioxidation · Chemical functional groups · Oxidative injury · *Tetrapleura tetraptera* · Trona (*kaun*)

Introduction

Trona, also known as potash (potassium carbonate), is an inorganic compound made up of crude mixture of minerals, salts, and impurities which include sand, clay, and metals such as iron, aluminum, potassium, silicon, magnesium, and titanium (Sodipo 1993). It is a hydrated sequicarbon of sodium carbonate and sodium bicarbonate (Na_2CO_3*$NaHCO_3$-$2H_20$) (Sodipo 1993). Calcites have been reported to be the major chemical constituent, with hanksite, halite, pirssonite, and borax present in low concentrations (Lu et al. 2005).

Trona is commonly referred to as *kaun* and *kanwa* in the southern and northern parts of Nigeria respectively and an indigenous food addictive for tenderizing legumes, vegetables, bone, and meat (Bankole et al. 2015; Okoye et al. 2016). Its folkloric use in the treatment of cough, toothache, stomach ache, diarrhea, and lactation has been reported (Sodipo 1993). However, there are concerns about its toxicity owing to its indiscriminate use (Ajiboye et al. 2015). Ajiboye et al. (2015) also reported that 400 mg/kg of potash may be toxic and could deplete the antioxidant system in rats' liver and kidney. Bamaiyi and Momoh (2010) established effects of 245 mg/kg of potash on gastrointestinal enzymes and small intestine. However, the trona material safety data sheet states that the oral LD_{50} for rats is 4090 mg/kg (TATA 2013).

Despite all the reports on the toxic effects of potash, there is dearth of information on the amelioration and attenuation of potash-induced organ damage.

The protective effects of medicinal plants particularly spices against oxidative injuries are well documented (Pai

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Kotebagilu et al. 2014; Asadi-Samani et al. 2015). These therapeutic effects have been attributed to their phytochemical constituents. Amongst such plants is *Tetrapleura tetraptera*, naturally distributed in the tropical areas of Africa (Aladesanmi 2007). *T. tetraptera* is commonly used as spice in the eastern and southern part of Nigeria. Its indigenous names amongst Nigerian tribes include *Uyayak* (Ibibio), *Edeminang* (Efik), *Oshosho* (Igbo), *Dawo* (Hausa), and *Aridan* (Yoruba). Its folkloric uses include the treatment of fever, jaundice, leprosy rheumatism, high blood pressure, inflammation, cancer, and diabetes (Atawodi et al. 2014). Its antidiabetic and anti-inflammatory activity has been reported (Ojewole and Adewunmi 2004). Its mineral constituents include potassium, zinc, calcium, phosphorous, and iron (Akin-Idowu et al. 2011). Its phytochemical constituents have been shown to consists of tannins, phenolics, saponins, alkaloids, steroids, and flavonoids (Ojewole and Adewunmi 2004; Akin-Idowu et al. 2011). Secondary metabolites isolated from *T. tetraptera* fruits include 7-hydroxy-6-methoxy-2H-1-benzopyran-2-one, 3-0-[ß-Dglucopyranosyl-2′-acetamido-2′- deoxy]-oleanolic acid (Aridanin), 3-[(2-acetamido-2-deoxy-ß-D-glucopyranosyl)oxy]-16α-hydroxyolean-12-en-28-oic acid, 3-{[O-ßD-galactopyranosyl-(1 → 4)-(2-acetamido-2-deoxy-ß-D-glucopyranosyl)oxy]}olean-12-en-28-oic, 3-{(O-ß-D-glucopyranosyl-(1 → 6)-(2-acetamido-2-deoxy-ß-Dglucopyranosyl)oxy}olean-12-en-28-oic, and 3-{[O-ß-Dglucopyranosyl-(1 → 6)-ß-D-glucopyranosyl]-oxy}-27-hydroxyolean-12-en-28-oic acid (Adesina et al. 2016).

To the best of our knowledge, we report for the first time the therapeutic potential of the ethanol extract of *T. tetraptera* fruit and peels against trona-induced oxidative injury in the hepatic, kidney, and intestinal tissues.

Materials and methods

Plant material

Fruits of *T. tetraptera* were purchased from local farmers at Benin City, Nigeria. They were washed and dehulled. The peels and fruit pulp were air-dried, pulverized, and subjected to ethanolic extraction. The extracts were concentrated *in vacuo* and stored in airtight containers respectively for further studies.

Fourier transform infrared spectroscopy analysis

The functional groups of the extracts were determined by scanning on FTIR spectrophotometer at room temperature (25–28 °C) at 300–4000 cm^{-1} spectral range. The functional groups were determined by comparing the peak frequencies to the IR spectroscopy correlation table.

Animals

Thirty-six male albino rats of Wistar strain weighing 180–200 g were used for the present study. They were reared at the Animal House of Bells University of Technology, Ota, Nigeria. The rats were acclimatized for 7 days on normal pelletized mouse chow, and water given ad libitum at room temperature with a 12-h light and dark cycle before the commencement of the experiment. The animals were maintained under the approval of the Animal Ethical Committee, Bells University of Technology, Ota, Nigeria, in accordance with the declaration of Helsinki.

Five groups of six rats each were pretreated with trona (500 mg/kg bw) for 7 days, while a sixth group was administered water only and served as normal control. Four of the pretreated groups were subjected to posttreatment with *T. tetraptera* extracts for 7 days, while the fifth served as negative control as depicted below:

Group 1: Normal control (water only)
Group 2: Trona only (500 mg/kg bw)
Group 3: Trona (500 mg/kg bw) + *T. Tetraptera* fruit extract (1000 mg/kg bw)
Group 4: Trona (500 mg/kg bw) + *T. Tetraptera* fruit extract (2000 mg/kg bw)
Group 5: Trona (500 mg/kg bw) + *T. Tetraptera* peel extract (1000 mg/kg bw)
Group 6: Trona (500 mg/kg bw) + *T. Tetraptera* peel extract (2000 mg/kg bw)

All treatments were orally administered via intubation. The rats were fasted overnight at the end of the experiment and sacrificed by cervical dislocation.

The choice of dose for trona was based on trona material safety data sheet (TATA 2013), while that of the extracts was based on previous reports (Effiong et al. 2006).

Preparation of blood serum

Blood was collected from each rat by cardiac puncture in plain bottles and centrifuged at 3000 rpm for 10 min. The serum (supernatant) was transferred into labeled sample bottles and stored at 4 °C until further analysis.

Hepatic enzymes biomarkers

Serum aspartate transaminase (AST) and alanine transaminase (ALT) levels were determined via commercial kits from Randox® Laboratories, UK, according to the manufacturer's protocol.

Preparation of tissue homogenates

The intestine, kidney, and liver were removed, rinsed in ice-cold 1.15% KCl solution, and weighed. They were homogenized in 20 mM phosphate buffer (pH 6.6) and centrifuged at 10,000 rpm for 15 min at 4 °C. The supernatant was collected and stored at − 20 °C.

Lowry's method was used in determining the total protein of the tissues, using bovine serum albumin (BSA) as standard (Lowry et al. 1951).

Determination of oxidative stress parameters

The tissues were assayed for malondialdehyde (MDA) level (Chowdhury and Soulsby 2002) and catalase (CAT) activity (Aebi 1983).

Histopathology

Hepatic tissues were sliced to a thickness of 3 mm and arranged in a tissue cassette. They were processed using an automated tissue processor (Leitz 2005 model) according to manufacturer's protocol.

The processed images were quantitatively analyzed via ImageJ plugin.

Statistical analysis

One-way analysis of variance (ANOVA) was used in analyzing the differences between groups with the aid of Statistical Package for Social Sciences (SPSS) software, SPSS Inc., Chicago, Standard version 10.0.1. Results were expressed as mean ± standard deviation. *P* values < 0.05 were considered statistically significant.

Results

FTIR spectroscopy of the extracts revealed amines, alcohols, carboxylic acids, esters, ethers, aromatics, alkanes, aldehydes, ketones, phenols, and amides as the functional groups present as depicted in Table 1.

Administration of trona led to significant ($p < 0.05$) increase in catalase activities in the studied tissues, with the intestinal tissue being the most prominent as depicted in Fig. 1. This was significantly ($p < 0.05$) reduced to near normal after treatment with *T. tetraptera* fruit and peel extracts respectively.

There was significant ($p < 0.05$) increase in MDA levels on administration of trona, portraying lipid peroxidation in the studied tissues as shown in Fig. 2. These levels were significantly ($p < 0.05$) suppressed after treating with *T. tetraptera* fruit and peel extracts to near normal.

An elevated level of serum hepatic biomarkers (ALT and AST) was observed in rats' serum after administration of trona as revealed in Figs. 3a, b. Treatment with *T. tetraptera* fruit and peel extracts led to significant ($p < 0.05$) reductions, except ALT levels of rats (group 6) treated with 2000 mg/kg bw of *T. tetraptera* peel extract (Fig. 3a).

Histopathology examination revealed injuries in the hepatic tissues of rats following administration of trona as shown in Fig. 4b. This is evident by the increased hepatic lesions/alterations (Fig. 5). These alterations were observed to decrease on treatment with *T. tetraptera* fruit and peel extracts as revealed in Figs. 4c–f and 5, with 2000 mg/kg bw and 1000 mg/kg bw of the fruit and peel extracts showing the best activities respectively.

Discussion

The influence of oxidative stress in the progression and pathogenesis of most degenerative diseases are well documented

Table 1 Chemical functional groups of *Tetrapleura tetraptera* ethanolic extracts

Functional group	Fruits (cm^{-1})	Peels (cm^{-1})	Chemical bonds
Aliphatic amines	1031.97	1031.94	C–N stretch
Aromatic amines, alcohols, carboxylic Acids, esters, ethers	1268.18	1267.98	N–O symmetric stretch; C–N stretch; C–O stretch
Nitro compounds; aromatics; alkanes	ND	1447.81	N–O asymmetric stretch; C–C stretch (in–ring); C–H bend
1° amines	1624.44	1614.90	N–H bend
α,β–unsaturated aldehydes, ketones	1688.30	1691.08	C=O stretch
Carboxylic acids	2939.41	2923.36	O–H stretch; $–CO_2H$
Alkynes (terminal); alcohols, phenols; 1°, 2° amines, amides	3326.81	3309.58	–C ≡ C–H: C–H stretch; O–H stretch, H–bonded; N–H stretch

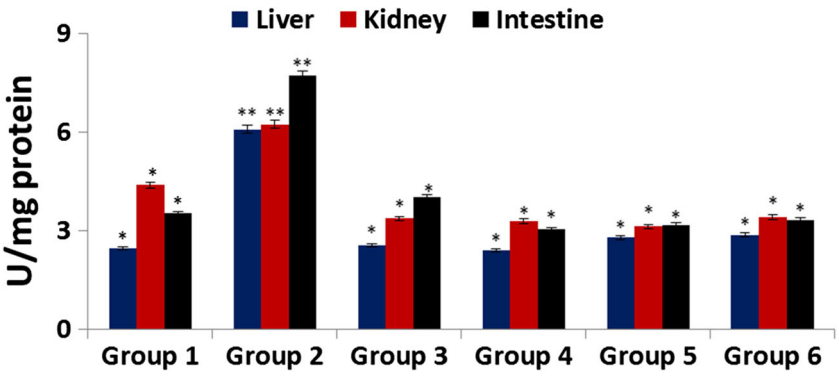

Fig. 1 Catalase activity in visceral organs of experimental groups. Data = mean + SD; $n = 6$. *Statistically significant compared to group 2; **statistically significant compared to group 1

(Erukainure et al. 2014; Schieber and Chandel 2014; Pisoschi and Pop 2015). This has been attributed to redox imbalance owing to elevated levels of free radicals that surpasses the body's endogenous antioxidant system, thereby leading to oxidative damages with cytotoxic consequences (Wang et al. 2014). The hepatic and intestinal tissues are of great importance, as they play a major role in the metabolism of food and make up the gastrointestinal (GI) system. Most food additives exhibit their toxicity when they are being digested. The kidney also functions in the elimination of ingested toxic by-products from the body, thus reducing their toxicity. A compromise in the antioxidant and membrane lipid integrity of these tissues poses a toxic detrimental threat. In this study, the oxidative effect of trona, a common food addictive, was examined in rat models as well as the antioxidant therapeutic effect of *T. tetraptera* ethanolic extract.

The increased catalase activities in hepatic, renal, and intestinal tissues after ingestion contradict previous reports of depleted activities in trona-induced toxicities (Ajiboye et al. 2015; Imafidon et al. 2016). González-Párraga et al. (2003) reported similar effects in yeast exposed to H_2O_2. Similar effects were reported in rats exposed to low-lipid diets (Erukainure et al. 2016). Increased catalase activity has been reported in oxidative stress in cigarette smoking-induced oxidative stress in the lungs (Rahman and MacNee 1999). These studies attributed the increased activity as response to oxidative stress. The reduced catalase activities to near normal in the studied tissues after treatment with the extracts thus suggest a protective effect against trona-induced oxidative injuries.

The increased MDA levels after ingestion of trona indicate an occurrence of lipid peroxidation. This is consistent with several studies on increased MDA levels in tissues due to induction of oxidative injuries (Noeman et al. 2011; Jain et al. 2015; Li et al. 2015). MDA has been reported to elicit multiple biological and toxicological effects (Long et al. 2009). The significant ($p < 0.05$) decreased levels after treatment with the extracts indicate an anti-peroxidative effect which can be attributed to the reported phytochemical constituents of the fruits and peels. Similarly, the identified functional groups of the extracts (Fig. 1a, b and Table 1) indicate their antioxidant functions particularly the phenols with reported antioxidant activities (Kähkönen et al. 1999; Balasundram et al. 2006; Palacios et al. 2011). The electron-deficient moieties of N–H bend, N–O symmetric C–C stretch, and C=O stretches portray a potent antioxidant, owing to the ability to attract additional electrons (Harrold and Zavod 2013). The presence of amines may contribute to the anti-peroxidative effect of the extracts, as MDA reacts with amines of tissue proteins to induce oxidative toxicity (Long et al. 2009). The amines present in the extracts can abate such reactions by reacting with MDA, thus protecting the tissue proteins.

Increased serum hepatic biomarkers have been reported in oxidative hepatic injury (Contreras-Zentella and Hernández-Muñoz 2016; Schaffer et al. 2016). The similar effect after

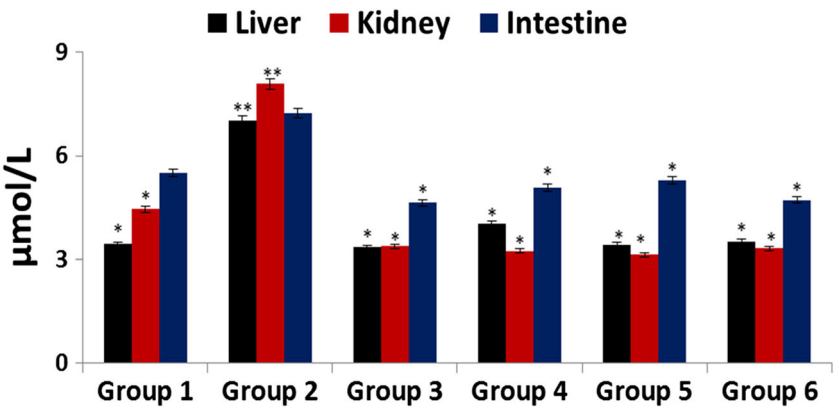

Fig. 2 MDA level in visceral organs of experimental groups. Data = mean + SD; $n = 6$. *Statistically significant compared to group 2; **statistically significant compared to group 1

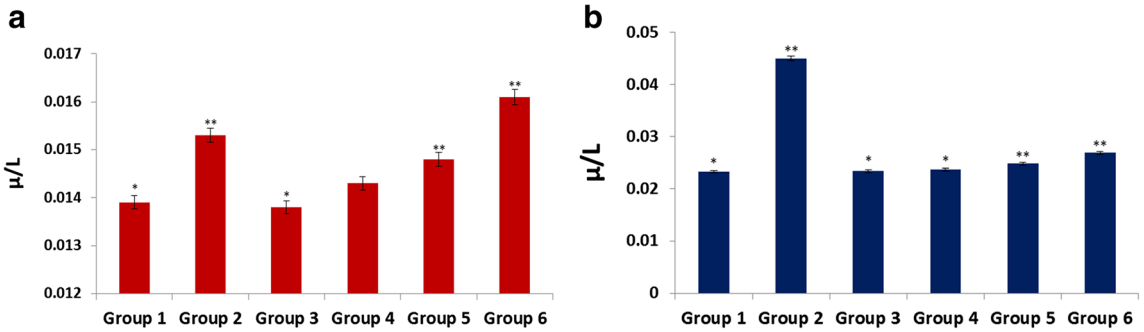

Fig. 3 **a** Serum ALT level of experimental groups. **b** Serum AST level of experimental groups. Data = mean + SD; $n = 6$. *Statistically significant compared to group 2; **statistically significant compared to group 1

ingestion of trona further indicates an occurrence of oxidative injury (Fig. 4a, b). Hepatic leakage of these enzymes has been attributed to inflammation of the liver, leading to disintegration of its plasma membrane (Onyema et al. 2006). This also correlates with the increased MDA level in trona-ingested rats, thus implicating its influence on the increased serum levels of the studied enzyme biomarkers (Figs. 3 and 4b). The reduced levels of these enzymes in rats treated with the extracts indicate a stabilizing effect on the hepatic plasma membrane and restoration of the membrane integrity. This can also be attributed to the synergetic effect of the phytochemical constituents and FTIR-identified chemical functional groups (Fig. 1a, b and Table 1).

The increased hepatic lesions/alterations after ingestion of trona further indicate an occurrence of oxidative hepatic injury which correlates with the high MDA level (Fig. 3a) and increased serum hepatic enzyme biomarkers (Fig. 4a, b). Lesions and alterations in hepatic tissues have been reported in oxidative stress (Richardson et al. 2010; Jarrar and Taib 2012). The reduced levels after

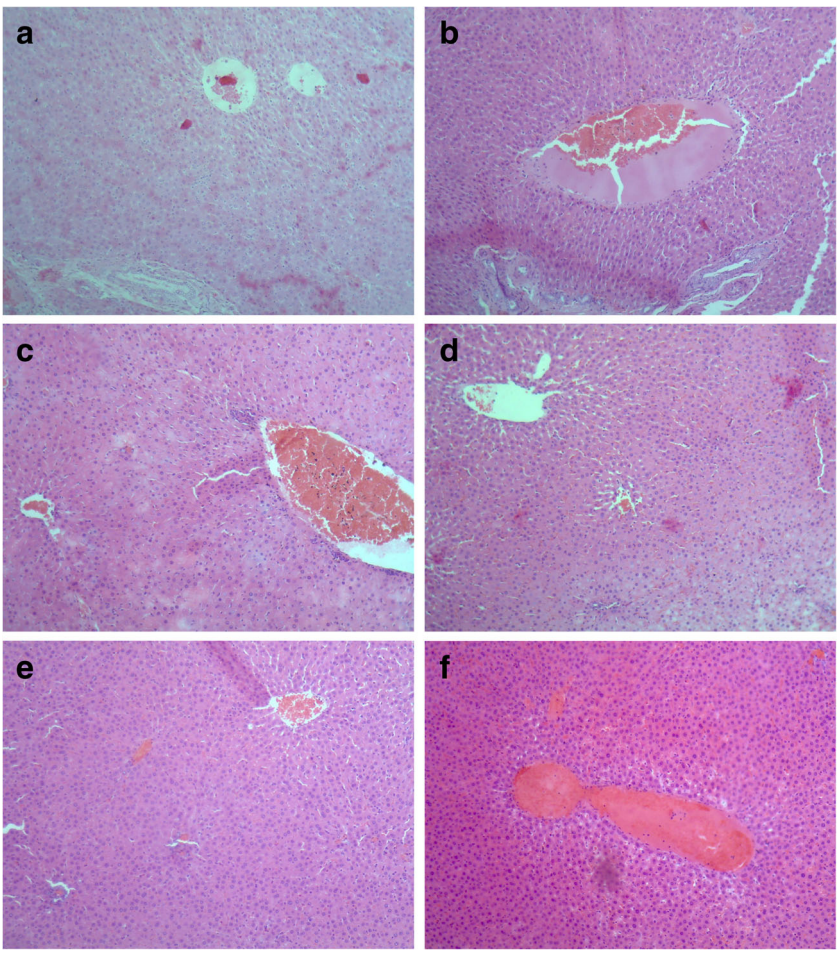

Fig. 4 Histopathological changes on the hepatic tissues of experimental groups

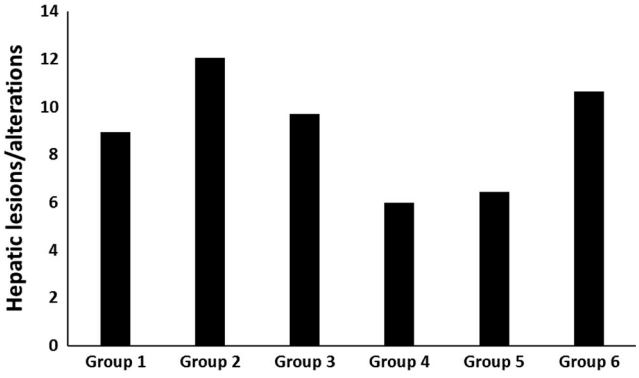

Fig. 5 Hepatic lesions/alterations of experimental groups. Values = $\times 10^5$

treatment with the extracts (Figs. 4c and 5) indicate their protective role against trona-induced oxidative hepatic injury, which correlates with the depleted levels of MDA (Fig. 3a) and serum hepatic enzyme biomarkers (Fig. 4a, b) respectively.

Conclusion

These results indicate the antioxidant protective effect of *T. tetraptera* against trona-induced oxidative injury. This can be attributed to the identified functional groups, with amine playing an influential role. Thus, the inclusion of this spice in meals is encouraged. Further studies on its molecular mechanism of action are being recommended.

Compliance with ethical standards All studies were carried out under the approval and guidelines of the biological ethical committee of the Animal Ethical Committee, Bells University of Technology, Ota, Nigeria, in accordance to the Declaration of Helsinki

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest The authors declare that they have no conflict of interest.

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